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10/811,694

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Ariffeen Bongso

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EXAMINER

TON, THAIAN N

ART UNIT

PAPER NUMBER

1632

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/811,694

Applicant(s)

BONGSO ET AL.

Examiner

Thaian N. Ton

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 76, 79, 80, 82-84 and 93-97 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 76, 79, 80, 82-84, 93-97 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Applicants' Amendment and Response, filed 2/27/07, has been entered. Claims 76, 80, 82-84, 93 are amended; claims 21-75, 77, 78, 81, 85-92 and 98-100 are cancelled; claims 76, 79, 80, 82-84, 93-97 are pending and under current examination.

#### *Election/Restrictions*

Applicant's election with traverse of Group IV (claims 76-79) in the reply filed on 6/12/06 is acknowledged. The traversal is on the ground(s) that the Examiner has not shown that the claimed inventions are independent and distinct, so as to justify the restriction requirement.

Applicants have cancelled claims that relate to Groups I-III.

#### *Priority*

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Australia (No. PR8028, PS0789, PS1812) and on September 28, 2001, February 28, 2002, and May 16, 2002, respectively. Applicants have provided a postcard to show that the certified copies have been accepted by the PTO, however, the Examiner responds that no certified copies are in the record. Applicants are requested to submit the certified copies again, if possible, in order to make the record complete and for the Examiner to determine Applicants' claim for foreign priority.

#### *Sequence Compliance*

Applicants' have now amended the specification to provide appropriate sequence identifiers for the sequences on page 39, lines 14 and 18. This objection is withdrawn.

*Claim Rejections - 35 USC § 112*

The prior rejection of claims 76 and 79-97, under 112, 1<sup>st</sup> paragraph is withdrawn in view of Applicants' amendment to the claims, which now recites obtaining a fibroblast feeder cell layer.

A new rejection appears below that is necessitated by Applicants' amendment to the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 76, 79, 80, 83, 84, 93 and 94 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A conditioned medium for deriving and culturing a human ES cell line in a substantially undifferentiated state comprising: obtaining human adult fallopian tubal (HAFT) fibroblast cells, culturing the HAFT cells in the presence of a medium selected from the group consisting of HES, KO, HES-KS, KO-HS, HFE, HM, HF, and HF-HS, and separating the medium from the cells to obtain conditioned medium.

The specification does not reasonably provide enablement for utilizing any type of human adult fibroblast feeder cell to produce a conditioned medium for deriving and culturing human ES cell lines. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the

specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

*Response to Applicants' Arguments.* Applicants have provided several arguments about their invention, with regard to the Examiner's previous rejection, under §102 and §103 with regard to the Xu publication. The Examiner addresses these arguments as pertinent to the instant rejection. In particular, Applicants have now amended the claims to recite utilizing adult fibroblast feeder cells to produce the conditioned medium. Applicants argue that all of the cell lines that are instantly claimed are adult skin, muscle or HAFT fibroblast feeder cells, which are derived from adult (newborn and older) primary tissue and are untransformed cells. See pages 6-7, bridging ¶.

Applicants point to Xu, who specifically states that, "[f]ibroblasts derived from adults are not generally used as feeder cells, suggesting that more mature cells lose their ability to provide factors requisite to support stem cell growth" (see page 7, 3<sup>rd</sup> full ¶ of the Response, as well as p. 3, ¶34 of Xu).

Thus, Examiner interprets this passage of Xu to read that adult fibroblast feeder cells *generally* do not support undifferentiated stem cell growth, as required in the instant invention. Given this passage of Xu, one of skill in the art would not be able to readily rely upon the art to support that any adult fibroblast feeder cell would provide a conditioned medium that would sufficiently maintain hES cells in an undifferentiated state. As such, the claimed invention is limited to the particular adult fibroblasts that are exemplified in the as-filed disclosure, human adult fallopian tubal (HAFT) fibroblast cells.

*Nature of the Invention.* The amended claims are directed to a conditioned medium for deriving and culturing a human ES cell line in a substantially undifferentiated state, prepared by obtaining a fibroblast feeder layer comprising

human adult fibroblast feeder cells which support the derivation and/or culture of human pluripotent ES cells in a substantially undifferentiated state, culturing the fibroblast feeder cell in the presence of a medium selected from the group consisting of HES, KO, HES-HS, KO-HS, HFE, HM, HF, HF-HS and separating the medium from the cells to obtain the medium.

*Breadth of the claims.* The breadth of the claims encompasses using any adult fibroblast feeder cell line to produce the conditioned medium.

*Guidance of the Specification/The Existence of Working Examples.* The specification teaches that human ES cells (hES) can only be maintained in an undifferentiated state on either irradiated or mitomycin-C treated mouse embryonic fibroblast feeder cells. The specification teaches methods of deriving and propagating hES cells in the absence of feeder cells. The specification teaches that cultured fibroblasts can be used in order to produce the conditioned medium (see page 21, lines 17-20), contemplating various cell lines including Detroit 551, MRC-5 or WI-38 (p. 22, lines 12-13), or other embryonic, fetal or adult skin or muscle feeder cells (p. 25, lines 1-5).

The working examples in the specification are directed to producing conditioned medium from mouse embryonic fibroblasts, human embryonic muscle, human embryonic skin, and adult human fallopian tubal fibroblast cells, (Example 1). The specification hES cells can maintain an undifferentiated state in the presence of MEF, adult fallopian tubal and human embryonic muscle and skin feeder fibroblast conditioned medium (p. 35, lines 5-10). The specification teaches that the human fetal muscle samples were prepared such that primary cultures of fibroblasts were established (see p. 36, lines 24-25); the description of all the figures show that the cells used as feeder cells are all fibroblast feeder cells (see Figure legends, pages 6-7).

*State of the Art/Predictability of the Art.* Xu *et al.* (cited previously) teach that adult fibroblast feeders are not generally used to culture stem cells, because

they appear to lose the ability to provide factors for stem cell growth. See Xu, p. 3, ¶34, and Applicants' Response. Thus, one of skill could not predictably rely upon the art for guidance with regard to utilizing the breadth of any human adult fibroblast feeders to produce conditioned medium to maintain hES cell lines in an undifferentiated state.

*The Amount of Experimentation Necessary.* The claims are not enabling for the following reasons:

The breadth of utilizing any adult fibroblast feeder cell to maintain hES cells in an undifferentiated state is not found to be predictable, because the state of the art shows that often, adult fibroblasts appear to lose their ability to produce the factors necessary to maintain hES cells in an undifferentiated state. See Xu *et al.*, who provide the state of the art at the time of filing.

Accordingly, in view of the lack of teaching or guidance provided by the instant specification, with regard to utilizing any adult fibroblast feeder cell to produce conditioned medium for deriving and culturing human ES cell lines in a substantially undifferentiated state, the unpredictable state of the art with regard to utilizing any adult fibroblast feeder cell line to maintain hES cells in an undifferentiated state, it would have required undue experimentation, for the skilled artisan, to practice the claimed invention.

Claims 94-97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

With regard to the instant invention, the only adult fibroblast cells that are used that can maintain hES cells in an undifferentiated state are HAFT cells (see p. 31, Example 1, line 7). Other claimed embodiments are not directed to adult

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fibroblast cells, the Detroit 551 cell line (claim 95) are fetal skin fibroblasts (see page 33, line 26 of the specification); the MRC-5 cell line (claim 96) is from fetal lung tissue (see p. 20, line 6 of the specification); the WI-38 cell line is from embryonic lung tissue (p. 20, line 7). Thus, the specification only provides guidance with regard to culturing hES cells with conditioned medium from HAFT fibroblast cells and does not provide any guidance for using the particular cell lines recited in claims 95-97, because these cell lines are not adult fibroblast cells.

Accordingly, one of skill in the art would have had to practice undue experimentation, with regard to the instantly claimed cell lines, in order to practice the claimed invention.

*Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 95-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is a new ground of rejection, necessitated by Applicants' amendment.

Claims 95-97 are indefinite because the metes and bounds of the claim cannot be determined. The claims recite that the feeder layer comprises the Detroit 551, MRC-5, or WI-38 cell lines (claims 95-97, respectively). However, these claims refer to claim 76, which requires adult fibroblast feeder cells. These cell lines are not adult fibroblast cells and thus, render the claims indefinite.

*Claim Rejections - 35 USC § 102*



The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 76, 79, 80, 82-84, 93-97 remain rejected under 35 U.S.C. 102(e) as being anticipated by Xu *et al.* (2002, of record).

*Applicants' Arguments.* Applicants argue that the claim 76 is now amended to recite that the fibroblast feeder layer comprises human adult fibroblast feeder cells, and that Xu *et al.* teach using fibroblast-like cells (derived from human ES cells). Applicants argue that the human "fibroblast-like cells" of the Xu reference are not the human adult fibroblast feeder cells employed in the present claims, and further, the adult fibroblast feeder cells would not have been exposed to surrounding tissues, as would the adult fibroblast feeder cells. Applicants argue further that the '117 publication teaches that adult fibroblast cells are not generally used as feeder cells, suggesting that more mature cells lose the ability to provide the factors required to support stem cell growth (p. 3, ¶ 34 of the Xu document, and pages 6-7 of the Response).

*Response to Arguments.* These arguments are not persuasive. The claims are directed to a conditioned medium, produced by a specific process. These are product-by-process claims. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or

alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In *re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing In *re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

In the instant case, Applicants have not provided any guidance to show that adult fibroblast feeders, which Applicants argue have been exposed to surrounding tissues, would produce a conditioned medium that is patentably distinct from the conditioned medium produced by the "fibroblast-liked cells" of Xu. In particular, the claims are directed to a conditioned medium; thus, if adult fibroblast feeder cells impart patentable weight to the product (*e.g.*, by providing a specific factor(s) not present in the prior art), then Applicants should provide arguments or evidence as to why these factor(s) would not be present in the conditioned medium of Xu.

Furthermore, it is reiterated that the claimed invention is directed to a conditioned medium, wherein the only requirement for the medium is that it can maintain hES cells in an undifferentiated state. Xu anticipate the claimed invention, because they a conditioned medium that can maintain hES cells in an undifferentiated state. The type of fibroblast cell that is used to produce the conditioned medium does not impart a discernable difference in the resultant media, because the resultant media fulfills the limitations of the claims.

Xu teach the culture of primate pluripotent stem (pPS) cells in the absence of feeder cells, using conditioned medium. See Abstract. They specifically teach that the cells can be human ES cells (see p. 2, ¶ 0014). The cells used to condition the

medium can be any cell line, and in particular embodiments, can be a human cell line with the characteristics of fibroblast or muscle cells (p. 2, ¶ 0015). They teach compositions of proliferating pPS cells, and cell lines made from these cells (p. 2, ¶ 0017). They teach differentiating human ES cells to produce fibroblast-like cells which were then used to condition medium to culture human ES cells (p. 3, ¶ 0036). They specifically teach the isolation of human ES cell from blastocysts, and the isolation of the inner cell masses of blastocysts in order to establish the ES cell lines. They teach that these cells are replated on MEF feeder layers, in fresh ES medium. See p. 6, ¶ 0070-0071. They teach that various extracellular matrix components can be used, including Matrigel (p. 7, ¶ 0082). They teach that human fibroblast-like cells are especially appropriate for producing the conditioned medium (p. 9, ¶ 0109). They teach that to condition the medium, various media can be used, such as KO DMEM (p. 10 ¶ 0118). They teach producing human feeder cell line (p. 17, Example 7), and culturing undifferentiated ES cells in feeder free conditions using conditioned medium from the human fibroblast feeder cells (Examples 8-9), and culturing undifferentiated ES cells on human fibroblast feeder cells (Example 10).

Accordingly, Xu anticipate the claims.

Claims 76, 79, 80, 82-84, 93-97 remain rejected under 35 U.S.C. 102(e) as being anticipated by Xu (2003, of record).

Applicants provide the same arguments as above regarding Xu. The Examiner has addressed these arguments above, and maintains that Xu anticipates the claimed invention.

Xu teach producing conditioned media for use in culturing primate pluripotent stem cells in an undifferentiated state (see Abstract). They specifically teach that the primate pluripotent stem cells can be human ES cells col. 3, lines 1-3). They teach that the cells used to condition the medium can be from a human

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cell line that has the characteristic of a human muscle or fibroblast cell (see p. 3, lines 4-13). They teach that the cells can be obtained any source, but include producing the cells from differentiating ES cells (col. 5, lines 43-48). They teach that the conditioned medium is prepared by culturing the cells in a medium and then harvesting the medium (col. 7, lines 56-58). They teach that media, such as KO DMEM can be used with the cells that are used to condition the medium (col. 7, lines 6-10 and 30-32).

Accordingly, Xu anticipate the claims because they teach a conditioned medium for maintain ES cells in a medium that has been conditioned with a human feeder layer, and separating the medium from the cells to obtain the medium.

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 76, 79, 80, 82-84, 93-97 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bodnar *et al.* (of record) when taken with Bongso *et al.* (of record).

*Applicants' Arguments.* Applicants argue that the claims are now directed to human adult fibroblast feeders, and Bodnar *et al.* do not teach using a human feeder cell for conditioning the media, therefore, Bodnar is no longer relevant to the instant claims (see p. 8, last ¶ of the Response). Applicants argue that the conditioned media of the claimed invention is directed to maintaining the cells in an undifferentiated state, whereas Bongo was only able to maintain the ICM-derived stem cells for two passages, and thus, this is not a cell line, as recited in the present claims (see page 9, 1<sup>st</sup> ¶).

*Response To Arguments.* Applicants' arguments have been considered, but are not persuasive. With regard to Bodnar *et al.*, the Examiner notes that it is the combination of the references, not solely the Bodnar reference that is used in this rejection. Bodnar does not teach using human feeder cells, as is acknowledged in the rejection. However, they teach producing conditioned medium to maintain ES cells in an undifferentiated state and provide sufficient motivation to modify their methods to produce a conditioned medium from human feeder layers. With regard to Applicants' arguments that Bongso was only able to maintain the ICM-derived cells for "two passages", Applicants are arguing limitations that are not within the claims. The claims do not require a specific amount of time in which the cells required to be cultured, the claims only require that the medium be used for deriving and culturing hES cell lines in an undifferentiated state.

With regard to Applicants' arguments that Bongso showed that two of the ICM clumps differentiated into fibroblasts, it is noted that these two clumps came from the same source, and the remaining 17 (from 8 different patients) produced "typical stem cell morphology". Thus, Bongso clearly teach that a majority of their ICM clumps were maintained in an undifferentiated state. It is maintained that

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the combination of the art provides the sufficient motivation and reasonable expectation of success.

Bodnar *et al.* teach the growth of primate-derived primordial stem cells by culturing the cells in a nutrient medium, and a substrate consisting of feeder cells, and an extracellular matrix component. See Abstract. They teach that primordial stem cells can be isolated from any source, including primates, and humans. The primordial stem cells that are contemplated by Bodnar include ES cells, as they teach that these cells are “totipotent” (see p. 1, lines 14-16, and p. 6, lines 7-9, section 3.1.10). The culture medium is effective to support the growth of the primordial stem cells (p. 2, lines 21-30) and can include various growth factors, that can be determined in order to maintain the primordial stem cells in an undifferentiated state (p. 4, lines 9-20). They teach that a conditioned medium can be made by supplementing with soluble factors derived from feeder cells (p. 5, lines 1-3 section 3.1.2). The cells can either be grown in the culture medium with feeder cells, or an extracellular matrix produced from the feeder cells (p. 7, lines 21-28). They teach that the fibroblast feeder cells can be from mouse, or other species (see p. 10, lines 1-2). They teach the isolation of the primate primordial stem cells (p. 11, section 3.2.2). They teach that the methods can be used to produce new primate stem cell lines (p. 14, section 3.4). In particular, they teach that conditioned medium was made, using mouse embryonic fibroblasts in ES cell medium. They teach the growth of primate-derived primordial stem cells on a fibroblast feeder layer and conditioned medium. See p. 19, section 4.1. They teach the growth of rhesus-derived ES cells without a feeder, using conditioned medium and a fibroblast matrix. See p. 2, section 4.2.

Bodnar *et al.* do not specifically teach using a human feeder cell for conditioning the media. However, prior to the time the claimed invention was made, Bongso *et al.* teach the development of human embryos to blastocyst stage on human tubal epithelial monolayers, and then after blastocyst formation, the

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hatched ICM and trophoblast were allowed to attach to the feeder monolayer. They further teach that healthy ICM lumps could be separated and grown *in vitro* (see Abstract). They teach that the ICM, if isolated, contain ES cells (see page 2110, 1<sup>st</sup>).

Accordingly, in view of the combined teachings of Bodnar and Bongso, it would have been obvious for one of skill in the art to modify the techniques to produce conditioned medium, as taught by Bodnar, to use a human cell line, as taught by Bongso, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make this modification, because Bongso clearly show that ES cells can be grown on human feeder layers, and provide motivation in stating that, "A feeder cell type similar to the species of the embryo may be more ideal than that of a heterologous species." See page 2116, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

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*Conclusion*

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tnt  
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Art Unit 1632

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*AV 1632*